



11-26-03

1646.

Attorney Docket No. 9233.46

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Ekwuribe et al.
Serial No.: 10/075,097
Filed: February, 13, 2002
For: Methods of Treating Diabetes Mellitus

Confirmation No.: 7253
Group Art Unit: 1646

November 25, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Attached is a list of documents on form PTO-1449 together with a copy of each identified document. It is requested that these documents be considered by the Examiner and officially made of record in accordance with the provisions of 37 C.F.R. § 1.56 and Section 609 of the MPEP.

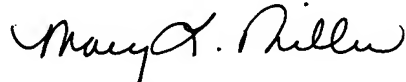
Also attached is a Declaration of James Gordon Still under 37 C.F.R. § 1.132 in which Dr. Still provides information about the slides that are included on the attached PTO Form 1449 as items 76 and 81. Although applicants provide these slides to the examiner in the interest of full disclosure in accordance with applicant's duty, it is applicants' belief that these slides are not "printed publications" as set forth in 35 U.S.C. § 102(b) and are thus not prior art to the claimed invention. Applicants base this belief on a comparison of the facts in this case as set forth in Dr. Still's Declaration with the facts set forth in *Regents of the University of California v. Howmedica, Inc.* [210 U.S.P.Q. 727 (D.N.J. 1981); *aff'd*, 676 F.2d 687 (3rd Cir. 1982); copy enclosed], in which the court determined that slides shown during an oral presentation did not constitute a "printed publication" within the meaning of 35 U.S.C. § 102(b). Because the facts reviewed by the court parallel the facts of the present application, applicants believe these slides

Attorney Docket No. 9233.46
Application Serial No. 10/075,097
Page 2 of 2

are not prior art against the invention as claimed in the present application.

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. § 1.97(b). Accordingly, no fee is believed due. However, the Commissioner is authorized to charge any deficiency or credit any refund to Deposit Account No. 50-0220.

Respectfully submitted,



Mary L. Miller
Registration No. 39,303

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
Post Office Box 37428
Raleigh, NC 27627
Telephone (919) 854-1400
Facsimile (919) 854-1401

CERTIFICATE OF EXPRESS MAILING UNDER 37 CFR §1.10

"Express Mail" mailing label number: EV 353594627 US Date of Deposit: November 25, 2003
I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.


Cathy A. Schetzina

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office				Attorney Docket Number 9233-46		Serial No. 10/075,097	
LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)							
Applicants: Ekwuribe et al.							
Filing Date February 13, 2002						Group 1646	
U. S. PATENT DOCUMENTS							
Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate	
	1. 2002/0160938	10/31/2002	Brandenburg et al.	A1			
	2. 2003/0144468	07/31/2003	Ekwuribe et al.	A1			
	3. 2003/0087808	05/08/2003	Soltero et al.	A1			
	4. 2003/0083232	05/01/2003	Soltero et al.	A1			
	5. 2003/0069170	04/10/2003	Soltero et al.	A1			
	6. 2003/0060606	03/27/2003	Ekwuribe et al.	A1			
	7. 2003/0050228	03/13/2003	Ekwuribe et al.	A1			
	8. 2003/0027995	02/06/2003	Ekwuribe et al.	A1			
	9. 2003/0004304	01/02/2003	Ekwuribe et al.	A1			
	10. 4,602,043	07/22/1986	Geho				
	11. 4,662,872	05/05/1987	Cané				
	12. 4,704,394	11/03/1987	Geho				
	13. 4,761,287	08/02/1988	Geho				
	14. 4,822,337	04/18/1989	Newhouse et al.				
	15. 4,863,896	09/05/1989	Geho et al.				
	16. 4,963,526	10/16/1990	Ecanow				
	17. 5,320,094	06/14/1994	Laube et al.	A			
	18. 5,321,009	06/14/1994	Baeder et al.	A			
	19. 5,364,838	11/15/1994	Rubsamen	A			
	20. 5,420,108	05/30/1995	Shohet	A			
	21. 5,468,727	11/21/1995	Phillips et al.	A			
	22. 5,597,797	01/28/1997	Clark et al.	A			
	23. 5,681,567	10/28/1997	Martinez et al.	A			

EXAMINER
*EXAMINER

DATE CONSIDERED

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through c. conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket Number
9233-46

Serial No.
10/075,097

LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants: Ekwuribe et al.

Filing Date
February 13, 2002

Group
1646

24.	5,704,910	01/06/1998	Humes	A		
25.	5,714,519	02/03/1998	Cincotta et al.	A		
26.	5,763,396	06/09/1998	Weiner et al.	A		
27.	5,843,866	12/01/1998	Weiner et al.	A		
28.	5,866,584	02/02/1999	Cincotta et al.	A		
29.	5,997,848	12/07/1999	Patton et al.	A		
30.	6,042,822	03/28/2000	Gilbert et al.	A		
31.	6,057,292	05/02/2000	Cunningham et al.	A		
32.	6,147,108	11/14/2000	Hauptman	A		
33.	6,342,225	01/29/2002	Jones et al.	B1		
34.	6,506,730	01/14/2003	Lee et al.	B1		

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation Yes No
35.	EP 0 511 903	10/14/1998	EP	B1		Claims
36.	99/65941	12/23/1999	WO	A1		

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

37.	Agarwal et al. "Polymethacrylate-based Microparticulates of Insulin for Oral Delivery: Preparation and In Vitro Dissolution Stability in the Presence of Enzyme Inhibitors" <i>International Journal of Pharmaceutics</i> 225:31-39 (2001)
38.	Allaudeen et al. "Orally Active Insulin: A Single Insulin Conjugate Selected for Future Studies" 60 th Annual Meeting of the American Diabetes Assoc., Atlanta, GA June 2000 (Abstract)
39.	Anderson et al. "HIM2, a Novel Modified Insulin, has Improved Systemic Pharmacokinetics in Normal Dogs, Compared to Unmodified Insulin" American Diabetes Association 62 nd Annual Meeting June 2002 (Abstract)
40.	Block, Lawrence H. "Pharmaceutical Emulsions and Microemulsions" <i>Pharmaceutical Dosage Forms: Disperse Systems</i> , Vol. 2, Ed. Lieberman et al. (1996)
41.	Bone et al. "Successful Treatment of an Insulin Dependent Rat Model of Human Type I Diabetes with Orally Active Insulin" Program and Abstracts, 4 th International Workshop on Lessons from Animal Diabetes, Omiya, Japan November 1994 (Abstract)
42.	Bone et al. "Successful Treatment of Type 1 Diabetes with Orally-Active Insulin: Studies in The Insulin Dependent BB/S Rat" Program and Abstracts, 55 th Annual Meeting of the American Diabetes Association, Atlanta Georgia, June 1995 (Abstract)

EXAMINER
*EXAMINER

DATE CONSIDERED

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office		Attorney Docket Number 9233-46	Serial No. 10/075,097
LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)		Applicants: Ekwuribe et al.	
		Filing Date February 13, 2002	Group 1646
43.	Brange and Volund "Insulin Analogs with Improved Pharmacokinetic Profiles" <i>Advanced Drug Delivery Reviews</i> 35:307-335 (1999)		
44.	Cleland et al. "Emerging Protein Delivery Methods" <i>Current Opinion in Biotechnology</i> 12:212-219 (2001)		
45.	Clement et al. "Effects of Multiple Doses of Orally Administered Hexyl Insulin M2 (HIM2) on Postprandial Blood Glucose (PPG) Concentrations in Type 1 Diabetic (T1) Patients" American Diabetes Association 62 nd Annual Meeting, June 2002 (Poster)		
46.	Clement et al. "Oral Insulin Product Hexyl-Insulin Monoconjugate 2 (HIM2) in Type 1 Diabetes Mellitus: The Glucose Stabilization Effects of HIM2" <i>Diabetes Technology & Therapeutics</i> 4(4):459-466 (2002)		
47.	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)		
48.	Dange et al. "Poly(alkyl cyanoacrylate) Nanospheres for Oral Administration of Insulin" <i>Journal of Pharmaceutical Sciences</i> 86(12):1403-1409 (Dec. 1997)		
49.	Dandona et al. "Effect of an Oral Modified Insulin on Blood Glucose Levels in Fasting and Fed Type 1 Diabetic Patients Receiving a "Basal" Regimen of Injected Insulin" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)		
50.	Ekwuribe et al. "Calcitonin Drug-Oligomer Conjugates, and Uses Thereof" U.S. Serial No. 10/166,355, filed 11/08/2002, including Preliminary Amendment dated 02/26/2003 and Supplemental Preliminary Amendment dated 03/31/2003		
51.	Ekwuribe et al. "Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same" U.S. Serial No. 09/873,797, filed 06/04/2001		
52.	Ekwuribe et al. "Oral Insulin Delivery: Hydrolyzable Amphiphilic Oligomer Conjugates Prolong Glucose Reduction" <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> 26:147-148 (1999)		
53.	Ekwuribe, Nnochiri "Conjugation-Stabilized Polypeptide Compositions, Therapeutic Delivery and Diagnostic Formulations Comprising Same, and Method of Making and Using the Same" <i>Biotechnology Advances</i> 14(4):575-576 (1996) (Abstract)		
54.	Hinds et al. "Synthesis and Characterization of Poly(ethylene glycol)-Insulin Conjugates" <i>Bioconjugate Chem.</i> 11:195-201 (2000)		
55.	Kipnes et al. "Control of Postprandial Plasma Glucose by an Oral Insulin Product (HIM2) in Patients with Type 2 Diabetes" <i>Emerging Treatments and Technologies</i> 26:2 (2003)		
56.	Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes" American Diabetes Association Annual Meeting (June 24, 2001) (Abstract)		
57.	Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 24, 2001) (Poster)		
58.	Kube, D.M. "Multitalented Proteins Play a Key Role in Therapeutics" <i>Genomics and Proteomics</i> (Sept. 2002)		
59.	Marschutz et al. "Oral Peptide Drug Delivery: Polymer-Inhibitor Conjugates Protecting Insulin from Enzymatic Degradation In Vitro" <i>Biomaterials</i> 21:1499-1507 (2000)		
60.	Musabayane et al. "Orally Administered, Insulin-Loaded Amidated Pectin Hydrogel Beads Sustain Plasma Concentrations of Insulin in Streptozotocin-Diabetic Rats" <i>Journal of Endocrinology</i> 164:1-6 (2000)		
61.	Pang, David C. "Bridging Gaps in Drug Discovery and Development" <i>Pharmaceutical Technology</i> 82-94 (Nov. 1998)		

 EXAMINER
 *EXAMINER

DATE CONSIDERED

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket Number
9233-46

Serial No.
10/075,097

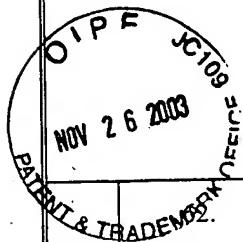
LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants: Ekwuribe et al.

Filing Date
February 13, 2002

Group
1646

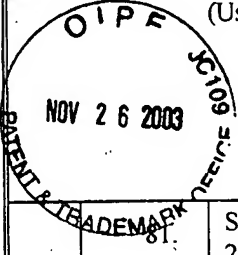


		Pauletti et al. "Improvement of Oral Peptide Bioavailability: Peptidomimetics and Prodrug Strategies" <i>Advanced Drug Delivery Reviews</i> 27:235-256 (1997)
63.		Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate HIM2" <i>AAPS Pharm. Sci.</i> 3(3) 2001 (Abstract)
64.		Radhakrishnan et al. "Chemical Modification of Insulin with Amphiphilic Polymers Improves Intestinal Delivery" <i>Proceed. Intl. Symp. Control. Rel. Bioact. Mater.</i> 25:124-125 (1998) (Abstract)
65.		Radhakrishnan et al. "Oral Delivery of Insulin: Single Selective Modification at B29-LYS With Amphiphilic Oligomer" Program and Abstracts, 1999 National Meeting of the Ameri. Assoc. Pharm. Scient., New Orleans, LA (1999) (Abstract)
66.		Radhakrishnan et al. "Structure-Activity Relationship of Insulin Modified with Amphiphilic Polymers" Program and Abstracts, 1998 National Meeting of the Amer. Assoc. Pharm. Scient., San Francisco, CA <i>Pharm. Sci.</i> 1(1):S-59 (1998) (Abstract)
67.		Radhakrishnan et al., "Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same" U.S. Serial No. 10/389,499, filed 03/17/2003
68.		Richards et al. "Self-Association Properties of Monomeric Insulin Analogs Under Formulation Conditions" <i>Pharmaceutical Research</i> 15(9):1434-1441 (1998)
69.		Shah and Shen "Transcellular Delivery of an Insulin-Transferrin Conjugate in Enterocyte-like Caco-2 Cells" <i>Journal of Pharmaceutical Sciences</i> 85(12):1306-1311 (1996)
70.		Sluzky et al. "Kinetics of Insulin Aggregation in Aqueous Solutions Upon Agitation in the Presence of Hydrophobic Surfaces" <i>Proc. Natl. Acad. Sci.</i> 88:9377-9381 (Nov. 1991)
71.		Soltero et al. "Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same" U.S. Serial No. 10/382,022, filed 03/05/2003
72.		Soltero et al. "Pharmaceutical Compositions of Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith" U.S. Serial No. 10/382,069, filed 03/05/2003
73.		Soltero et al. "Pharmaceutical Compositions of Insulin Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith" U.S. Serial No. 10/382,155, filed 03/05/2003
74.		Song et al. "Direct Measurement of Pulsatile Insulin Secretion from the Portal Vein in Human Subjects" <i>Journal of Clinical Endocrinology & Metabolism</i> 85(12):4491-4499 (2000)
75.		Still and McAllister "Effects of Orally Active Modified Insulin in Type 1 Diabetic Patients" <i>Clinical Pharmacol. Therap.</i> 69(2): P95 (Feb. 2001) (Abstract)
76.		Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Slide Presentation 2001 Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001
77.		Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" 2001 Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 (Handout)
78.		Still et al. "Magnitude and Variability of Pharmacokinetic and Glucodynamic Responses to Modified Human Insulin Administered Orally to Healthy Volunteers" <i>Diabetes Research and Clinical Practice</i> 56:S77 (2002)
79.		Still et al. "Methods of Reducing Hypoglycemic Episodes in the Treatment of Diabetes Mellitus" U.S. Serial No. 10/461,199, filed 06/13/2003
80.		Still, J. Gordon "Development of Oral Insulin: Progress and Current Status" <i>Diabetes/Metabolism Research and Reviews</i> , 18(1):S29-S37 (2002)

EXAMINER
*EXAMINER

DATE CONSIDERED

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)		Attorney Docket Number 9233-46	Serial No. 10/075,097
		Applicants: Ekwuribe et al.	
		Filing Date February 13, 2002	Group 1646
	81.	Still, J. Gordon "Oral Insulin Development" Slide Presentation, VI International St.Barts Symposium Diabetes 2000: Therapy and Technology, London, England, May 12, 2000	
	82.	Stocklin et al. "A Stable Isotope Dilution Assay for the In Vivo Determination of Insulin Levels in Humans by Mass Spectrometry" <i>Diabetes</i> 46(1):1-7 (Jan. 1997)	
	83.	Tyle, Praveen "Iontophoretic Devices for Drug Delivery" <i>Pharmaceutical Research</i> 3(6):318-326 (1986)	
	84.	Uchio et al. "Site-Specific Insulin Conjugates with Enhanced Stability and Extended Action Profile" <i>Advanced Drug Delivery Reviews</i> 35:289-306 (1999)	
	85.	Vreeland et al. "Molar Mass Profiling of Synthetic Polymers by Free-Solution Capillary Electrophoresis of DNA-Polymer Conjugates" <i>Anal. Chem.</i> 73(8):1795-1803 (2001)	
	86.	Ziy and Bendayan "Intestinal Absorption of Peptides Through the Enterocytes" <i>Microscopy Research and Technique</i> 49:346-352 (2000)	

EXAMINER

DATE CONSIDERED

*EXAMINER

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.